

DDK Docket No. 478.1063

What is claimed is:

1. A method for treating sexual dysfunction via inhalation, comprising:
inhaling a dose of from about 100 to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt).
2. The method of claim 1, wherein the sexual dysfunction is erectile dysfunction.
3. The method of claim 1, wherein the sexual dysfunction is female sexual dysfunction.
4. The method of claim 1, wherein the erectile dysfunction is psychogenic.
5. The method of claim 1, wherein the erectile dysfunction is organic.
6. The method of claim 1, wherein the dose comprises from about 200 micrograms to about 1600 of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt).
7. The method of claim 1, wherein the dose comprises from about 300 micrograms to about 1200 of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt).
8. The method of claim 1, wherein the dose comprises from about 400 micrograms to about 800 of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt).
9. The method of claim 8, wherein the sexual dysfunction is erectile dysfunction.
10. The method of claim 1, wherein the dose comprises from about 400 micrograms to about 1200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt).

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11. The method of claim 10, wherein the sexual dysfunction is erectile dysfunction.
12. The method of claim 1, wherein dose is a powder composition, and the powder composition includes said apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt) and a carrier material.
13. The method of claim 12, wherein the dose includes from about 400 to about 800 micrograms of apomorphine hydrochloride.
14. The method of claim 13, wherein the dose provides, in vivo, a mean Cmax of from about 0.7 ng/ml to about 2 ng/ml.
15. The method of claim 14, wherein the dose provides, in vivo, a mean plasma level of said apomorphine at seventy minutes after administration of from about 0.2 ng/ml to about 0.6 ng/ml.
16. The method of claim 13, wherein the apomorphine is apomorphine hydrochloride and at least 99% of said apomorphine hydrochloride has a particle size of 5 microns or less.
17. The method of claim 1, wherein the dose comprises a powder composition which includes apomorphine or a pharmaceutically acceptable salt or ester thereof and an anti-adherent material.
18. The method of claim 1, wherein the dose comprises a solution pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof, HFA134a, ethanol, and water.
19. The method of claim 18, wherein said water is present in an amount from greater than 2% by weight to about 10% by weight of the solution pMDI formulation.
20. The method of claim 1, wherein the dose comprises a suspension pMDI formulation

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including apomorphine or a pharmaceutically acceptable salt or ester thereof and a propellant which includes HFA134a and HFA227.

21. The method of claim 20, wherein the propellant includes about 60% by weight HFA134a and about 40% by weight HFA227.

22. A method for treating sexual dysfunction, comprising:

inhaling a dose including apomorphine or a pharmaceutically acceptable salt or ester thereof, said dose being sufficient to provide a therapeutic effect in about 10 minutes or less.

23. The method of claim 22, wherein the dose comprises a powder composition which includes apomorphine or a pharmaceutically acceptable salt or ester thereof and a carrier material.

24. The method of claim 23, wherein the carrier material is lactose and the apomorphine is apomorphine hydrochloride.

25. The method of claim 22, wherein the dose comprises a powder composition which includes apomorphine or a pharmaceutically acceptable salt or ester thereof and an anti-adherent material.

26. The method of claim 22, wherein the dose comprises a solution pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof, HFA134a, ethanol, and water.

27. The method of claim 26, wherein said water is present in an amount from greater than 5% by weight to about 10% by weight of the solution pMDI formulation.

28. The method of claim 22, wherein the dose comprises a suspension pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof and a propellant which includes HFA134a and HFA227.

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29. The method of claim 28, wherein the propellant includes about 60% by weight HFA134a and about 40% by weight HFA227.
30. The method of claim 23 wherein the powder composition further includes a force control additive.
31. The method of claim 30, wherein the force control additive is provided in an amount from about 0.15% to about 5% of the composition, by weight.
32. The method of claim 30, wherein the force control additive is selected from the group consisting of leucine, magnesium stearate, lecithin, and sodium stearyl fumarate.
33. The method of claim 30, wherein the force control additive includes leucine.
34. A method for treating sexual dysfunction via inhalation, comprising inhaling a dose of a powder composition into the lungs of a patient, the dose of the powder composition delivering, in vitro, a fine particle dose of from about 100 micrograms to about 1600 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt), when measured by a Multistage Liquid Impinger, United States Pharmacopeia 26, Chapter 601 Apparatus 4 (2003).
35. The method of claim 34, wherein the dose delivers, in vitro, a fine particle dose of from about 200 micrograms to about 1000 micrograms of said apomorphine when measured by a Multistage Liquid Impinger, United States Pharmacopeia 26, Chapter 601 Apparatus 4 (2003).
36. The method of claim 34, wherein the dose delivers, in vitro, a fine particle dose of from about 200 micrograms to about 800 micrograms of said apomorphine when measured by a Multistage Liquid Impinger, United States Pharmacopeia 26, Chapter 601 Apparatus 4 (2003).

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37. The method of claim 34, wherein the dose delivers, in vitro, a fine particle dose of from about 200 micrograms to about 600 micrograms of said apomorphine when measured by a Multistage Liquid Impinger, United States Pharmacopeia 26, Chapter 601 Apparatus 4 (2003).

38. The method of claim 34, wherein the dose delivers, in vitro, a fine particle dose of from about 200 to about 400 micrograms of said apomorphine when measured by a Multistage Liquid Impinger, United States Pharmacopeia 26, Chapter 601 Apparatus 4 (2003).

39. The method of claim 1, wherein the dose comprises a solution pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof, HFA 227, ethanol, and water.

40. The method of claim 39, wherein the solution pMDI further includes HFA134a.

41. The method of claim 22, wherein the dose comprises a solution pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof, HFA 227, ethanol, and water.

42. The method of claim 41, wherein the solution pMDI further includes HFA134a.

43. The method of claim 1, wherein the dose comprises a solution pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof and a CFC propellant.

44. The method of claim 1, wherein the dose comprises a suspension pMDI formulation including apomorphine or a pharmaceutically acceptable salt or ester thereof and a CFC propellant.

45. A method of treating sexual dysfunction, comprising inhaling a dose of a powder composition, the powder composition comprising from about 100 to about 3200 micrograms

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of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt).

46. The method of claim 45, wherein the powder composition further includes a carrier.

47. The method of claim 45, wherein the step of inhaling comprises:

entraining the powder composition in a gas flow upstream from an inlet port of a vortex chamber having a substantially circular cross-section,

directing the gas flow through the inlet port into the vortex chamber in a tangential direction;

directing the gas flow through the vortex chamber so as to aerosolise the powder composition; and

directing the gas flow with the powder composition out of the vortex chamber in an axial direction through an exit port, wherein a velocity of the gas flow at a distance of 300 mm outside of the exit port is less than a velocity of the gas flow at the inlet port.

48. The method of claim 46, wherein the powder composition comprises agglomerated particles, and the step of inhaling comprises:

entraining the agglomerated particles in a gas flow upstream from an inlet port of a vortex chamber,

directing the gas flow through the inlet port into the vortex chamber;

depositing the agglomerated particles onto one or more walls of the vortex chamber;

applying, via the gas flow through the vortex chamber, a shear to the deposited agglomerated particles to deagglomerate said particles,

directing the gas flow, including the deagglomerated particles, out of the vortex chamber, wherein a velocity of the gas flow at a distance of 300 mm outside of the exit port is less than a velocity of the gas flow at the inlet port.

49. The method of claim 46, wherein the carrier material has an average particle size of from about 40 microns to about 70 microns, and at least 90% of said apomorphine having a particle size of 5 microns or less.

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50. The method of claim 49, wherein the powder composition comprises agglomerated particles, and the step of inhaling comprises:

- entraining the agglomerated particles in a gas flow,
- depositing the agglomerated particles onto one or more surfaces;
- applying, via the gas flow, a shear to the deposited agglomerated particles to deagglomerate said particles.

51. The method of claim 45, wherein the step of inhaling comprises:

- generating an air flow through an inlet port of a chamber, the air flow having entrained therein the powder composition;
- directing the air flow through the chamber, the chamber having an axis and a wall curved about the axis, the air flow rotating about the axis; and
- directing the air flow through an exit port of the chamber,
- wherein a direction of the air flow through the inlet port is tangential to the wall, and a direction of the air flow through the exit port is parallel to the axis,
- and wherein a cross-sectional area of the air flow through the chamber is in a plane normal to the air flow and decreases with increasing distance from the inlet port.

52. An inhaler for producing an inhalable aerosol of a powdered apomorphine composition comprising

- an aerosolising device in the form a vortex chamber of substantially circular cross-section having a substantially tangential inlet port and a substantially axial exit port, wherein the ratio of the diameter of the vortex chamber to the diameter of the exit port is between 4 and 12;

- one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

- an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

53. An inhaler for producing an inhalable aerosol of a powdered apomorphine composition comprising an aerosolising device in the form of a vortex chamber of substantially circular cross-section having a substantially tangential inlet port,

wherein the inlet port has an outer wall which defines the maximum extent of the inlet port in the radially outward direction of the vortex chamber,

the extent of the outer wall in the axial direction of the vortex chamber is substantially equal to the maximum extent of the inlet port in the axial direction of the vortex chamber, and

the outer wall is substantially parallel with a wall of the vortex chamber;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

54. An inhaler for producing an inhalable aerosol of a powdered apomorphine composition comprising

an aerosolising device in the form of a vortex chamber of substantially circular cross-section having a substantially tangential inlet port, an exit port spaced from the inlet port in an axial direction, and a bottom surface which defines the furthest extent of the vortex chamber from the exit port in the axial direction, wherein the bottom surface further defines the furthest axial extent of the inlet port from the exit port,

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

55. An inhaler for producing an inhalable aerosol of a powdered apomorphine composition comprising

an aerosolising device in the form of a vortex chamber of substantially circular cross-section having a substantially tangential inlet port and an inlet conduit arranged to supply a powdered composition entrained in a gas flow to the inlet port, in use, wherein the cross-sectional area of the inlet conduit decreases towards the vortex chamber;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the inlet conduit with the powder composition in the received blister.

56. An inhaler for producing an inhalable aerosol of a powdered apomorphine composition comprising

an aerosolising device in the form of a vortex chamber of substantially circular cross-section having a substantially tangential inlet port and an arcuate inlet conduit arranged to supply a powdered composition entrained in a gas flow to the inlet port, in use;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the inlet conduit with the powder composition in the received blister.

57. An inhaler comprising:

a chamber having a top portion, a bottom portion, and a substantially cylindrical center portion, the chamber having an inlet port tangential to the center portion, the top portion having an exit port, wherein a ratio of a diameter of the chamber to a diameter of the exit port is between 4 and 12;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine

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or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

58. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising:

a chamber having a top portion, a bottom portion, and a cylindrical center portion, the chamber having an inlet port tangential to the cylindrical center portion, the chamber having an exit port in the top portion, wherein a length of the exit port is less than a diameter of the exit port;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

59. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising

an aerosolising device having formed therein, a chamber of substantially circular cross-section, the chamber having a substantially planar top surface, a substantially planar bottom surface, and a curved lateral surface, the aerosolising device including an inlet port, the inlet port extending from an outer surface of the aerosolising device to the chamber, the inlet port being tangential to the curved lateral surface, the aerosolising device further including an outlet port, the outlet port extending from the outer surface of the aerosolising device to the planar top surface of the chamber;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

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an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

60. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising

an aerosolising device defining a vortex chamber of substantially circular cross-section having a tangential inlet port, the aerosolising device including a vortex chamber wall defining a radially outer boundary of the vortex chamber and defining a maximum extent of the inlet port in a radially outward direction of the vortex chamber;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

61. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising:

an aerosolising device defining a vortex chamber of substantially circular cross-section having a tangential inlet port, an exit port spaced a distance apart from the inlet port in an axial direction, the aerosolising device including a vortex chamber bottom surface defining a furthest extent of the vortex chamber from the exit port in an axial direction and a furthest axial extent of the inlet port.

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

62. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler

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comprising:

an aerosolising device defining a vortex chamber of substantially circular cross-section having a tangential inlet port; and

an inlet conduit arranged to supply a powdered composition entrained in a gas flow to the inlet port, wherein a cross-sectional area of the inlet conduit decreases towards the vortex chamber;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the inlet conduit with the powder composition in the received blister.

63. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising:

an aerosolising device defining a vortex chamber of substantially circular cross-section having a tangential inlet port; and

an arcuate inlet conduit arranged to supply the powdered composition entrained in a gas flow to the inlet port;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the inlet conduit with the powder composition in the received blister.

64. An inhaler for producing an inhalable aerosol of a powdered medicament comprising an aerosolising device in the form of a vortex chamber having an axis and being defined, at least in part, by a wall which forms a curve about the axis, the vortex chamber having a cross-sectional area in a plane bounded by the axis, the plane extending in one direction radially from the axis at a given angular position (θ) about the axis,

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wherein the vortex chamber has a substantially tangential inlet port and a substantially axial exit port, and

said cross-sectional area of the vortex chamber decreases with increasing angular position (θ) in the direction, in use, of gas flow between the inlet port and the exit port;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

65. An inhaler for producing an inhalable aerosol of a powdered composition comprising an aerosolising device in the form of a vortex chamber having an axis and being defined, at least in part, by a wall which forms a curve about the axis, the vortex chamber having a substantially tangential inlet port and a substantially axial exit port, wherein the vortex chamber is further defined by a base, and the distance (d) between the base and a plane which is normal to the axis and is located on the opposite side of the base to the exit port increases with radial position (r) relative to the axis;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

66. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising:

a chamber defined by a top wall, a bottom wall, and a lateral wall, the lateral wall being curved about an axis which intersects the top wall and the bottom wall, the chamber enclosing a cross-sectional area defined by the axis, the top wall, the bottom wall and the lateral wall;

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the chamber having an inlet port and an outlet port, the inlet port being tangent to the lateral wall, the outlet port being co-axial with the axis, the cross-sectional area decreasing with increasing angular position from the inlet port in a direction of a gas flow through the inlet port;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

67. An inhaler for producing an inhalable aerosol of a powdered composition, the inhaler comprising:

a chamber including a wall, a base, an inlet port and an exit port, the chamber having an axis that is co-axial with the exit port and intersects the base, the wall being curved about the base, the inlet port being tangential to the wall, a height between the base and a plane normal to the axis at the exit port decreasing as a radial position from the axis to the inlet port increases;

one or more sealed blisters, each blister containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt);

an input for removably receiving one of the blisters, said inhaler, upon actuation, coupling the tangential inlet port with the powder composition in the received blister.

68. A drug loaded blister comprising

a base having a cavity formed therein, the cavity containing a powder composition including a carrier material and from about 100 micrograms to about 3200 micrograms of apomorphine or a pharmaceutically acceptable salt or ester thereof (based on the weight of the hydrochloride salt), the cavity having an opening which is sealed by a rupturable covering.

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69. The method of claim 46, wherein the powder composition comprises agglomerated particles, and the step of inhaling comprises:

entraining the agglomerated particles in a gas flow upstream from an inlet port of a vortex chamber,

directing the gas flow through the inlet port into the vortex chamber;

depositing the agglomerated particles onto one or more walls of the vortex chamber;

applying, via the gas flow through the vortex chamber, a shear to the deposited agglomerated particles to deagglomerate said particles,

directing the gas flow, including the deagglomerated particles, out of the vortex chamber to provide an ultrafine particle fraction, when measured by an Andersen Cascade Impactor, United States Pharmacopeia 26, Chapter 601 Apparatus 3 (2003), of at least about 70%.

70. The method of claim 45, wherein the step of inhaling comprises inhaling a dose having an ultrafine particle fraction, when measured by an Andersen Cascade Impactor, United States Pharmacopeia 26, Chapter 601 Apparatus 3 (2003), of at least about 70%.

71. The method of claim 46, wherein the step of inhaling comprises inhaling a dose having an ultrafine particle fraction, when measured by an Andersen Cascade Impactor, United States Pharmacopeia 26, Chapter 601 Apparatus 3 (2003), of at least about 70%.

72. The method of claim 45, wherein the step of inhaling comprises inhaling a dose having a fine particle fraction, when measured by an Andersen Cascade Impactor, United States Pharmacopeia 26, Chapter 601 Apparatus 3 (2003), of at least about 80%.

73. The method of claim 46, wherein the step of inhaling comprises inhaling a dose having a fine particle fraction, when measured by an Andersen Cascade Impactor, United States Pharmacopeia 26, Chapter 601 Apparatus 3 (2003), of at least about 80%.